REMARKS

The Office Action of March 11, 2003 has been reviewed and the Examiner's comments carefully considered. Claims 36-61 are currently pending in this application. Claims 48 and 50 are cancelled, claim 36 is amended, and claims 39, 41-47 and 58-61 are withdrawn from consideration by the Examiner. Support for the language of claim 36 is found on page 5, lines 21-24. No new matter has been added.

The Examiner asserts that newly submitted claims 36-61 are directed to an invention that is independent or distinct from the invention originally claimed assertedly because each of the peptides described as TC-1, TC-1*, TC-2, TC-la-d, rMTC-1*, rMTC-2, rYTC-1, and rYNAP-1 are directed to patentably distinct and/or independent peptides, and that claims 58-61 add methods for the preparation of a medicament, release systems and microbial peptides that are outside the scope of the original presentation of the claims. Claim 36 has now been amended to recite an "isolated microbicidal peptide that exhibits bactericidal and/or fungicidal activity having an amino acid sequence consisting essentially of the amino acid sequence of TC-1..." Claims 39 and 41-47 depend from claim 36. Applicants therefore respectfully request rejoinder of claims 39 and 41-47 based on the fact that the above-recited new, isolated, or recombinantly prepared peptides are no longer claimed in open-ended claims, all have similar sequences and, as now claimed, the peptides all exhibit antibacterial and/or antifungal activity which can be used in the treatment of infections in humans and animals. Therefore, based on the similarity of their sequences and their antimicrobial activity, the isolated microbicidal peptides of the claimed invention are not patentably distinct and/or independent peptides.

Furthermore, because claim 36 now recites that the isolated peptide of the invention has microbicidal and/or fungicidal activity, claim 36 now provides the requisite scope for the methods recited in claims 58-61.

Claims 36-38, 40 and 52-55 stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Daly et al. The Examiner asserts that Daly et al. discloses recombinant CXC chemokines whose amino acid sequences comprise the same amino acid sequence of TC-1 and TC-2. The Examiner also asserts that Daly et al. describes these CXC chemokines as small inducible proteins having a specific arrangement of four position-invariant cysteine residues in their primary amino acid sequence that form two disulfide bonds.

Applicants submit that the rejection of claims 36-38, 40 and 52-55 over Daly et al. is believed to be overcome by pointing out that claim 36 has now been amended to include the transitional phrase "*consisting essentially of*," which limits claim 36 to those amino acid sequences recited therein plus other amino acid sequences whose presence would not materially affect the action of the recited peptides. As the Examiner recognizes, Daly et al. does not teach TC-1, but rather a sequence that "comprises at least the amino acid sequence of TC-1." Claim 36, as now amended, is limited to the amino acid sequences recited therein and therefore is not anticipated by Daly et al. Furthermore, it has surprisingly been found that potent antimicrobial peptides, in particular peptides with a direct microbicidal activity, can be obtained by minor modifications of the well-known chemokines CTAP-III and NAP-2. TC-1* has, for example, been proven to be a potent microbicidal agent by deleting the two C-terminal amino acids of the chemokine

NAP-2, whereas TC-2 has been proven to be a direct microbicidal agent only by deleting the two C-terminal amino acids of the chemokine CTAP-III. These minor structural differences result in dramatic changes in activity of the compounds involved, and the Daly et al. structures of NAP-2 and CTAP-III do not teach or suggest the structures of the claimed microbicidal peptides. Because claims 37, 38, 40 and 52-55 depend from claim 36, directly or indirectly, they are similarly not anticipated by the Daly et al. reference.

Claims 36, 38, and 48-56 stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Baggiolini et al. The Examiner states that comparison of the sequences disclosed in the Baggiolini et al. specification shows that NAP-2 is 97% identical to TC-1, differing from TC-1 by the presence of two additional amino acids on the N-terminus, thus fully comprising the TC-1 sequence. Again, Applicants point out that claim 36, as now amended, recites that the isolated peptide of the invention *consists essentially of* the amino acid sequence of TC-1, thus limiting the isolated peptide to the exact amino acid sequences recited therein or other sequences which would not materially affect their precise action. These sequences as now claimed are neither taught nor suggested by Baggiolini et al. Because claims 38 and 48-56 depend from claim 36, directly or indirectly, they are also not anticipated by Baggiolini et al.

Claims 36, 38, and 48-57 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Baggiolini et al. in view of Cimbollek et al. The Examiner states that the Baggiolini et al. sequence of NAP-2 is 97% identical to TC-1 and that, although Baggiolini et al. does not disclose the NAP-2 for the treatment of bacterial and fungal endocarditis, Cimbollek et al. teach that both fungal and bacterial

infections are associated with endocarditis, thus it would have been obvious to treat endocarditis with the above chemokine due to its known antimicrobial activity. Applicants submit that the new and unexpected antimicrobial activity of the claimed invention inheres in the amino acid sequences as now more narrowly claimed. These sequences are neither taught nor suggested by Baggiolini et al., alone or in combination with Cimbollek et al., nor would it be obvious to modify the sequences of the claimed invention to generate the sequences disclosed by Baggiolini et al. As stated above, antimicrobial peptides, in particular peptides with a direct microbicidal activity, can be obtained by minor modifications of the well-known chemokines CTAP-III and NAP-2. TC-1* has been proven to be a potent microbicidal agent by deleting the two C-terminal amino acids of the chemokine NAP-2, and TC-2 has been proven to be a direct microbicidal agent only by deleting the two C-terminal amino acids of the chemokine CTAP-III. These minor structural differences result in dramatic changes in the activity of these compounds. Applicants submit, therefore, that the Baggiolini et al. and Cimbollek et al. references do not teach or suggest, alone or in combination, the structures of the claimed microbicidal peptides. Because claims 38 and 48-57 depend from claim 36, directly or indirectly, they are also non-obvious over Baggiolini et al. in view of Cimbollek et al.

Claims 37, 40 and 52-55 stand rejected under 35 U.S.C. § 112 for asserted indefiniteness. The Examiner states that claim 36 provides no antecedent basis for limitations in the claims that would modify SEQ ID NO: 12. Claim 36 has been amended to specifically claim an "isolated microbial peptide...consisting essentially of the amino

acid sequence of TC-1," thus now providing antecedent basis for the claim limitations contained in claims 37, 40 and 52-55.

Applicants respectfully submit that amended claim 36 is proper for entry after a Final Office Action because the amendment to the claim does not change the substantive content therein and therefore does not require any additional searching by the Examiner.

For all the foregoing reasons, claims 36-61 are patentable over the cited prior art and in condition for allowance. Reconsideration of the rejections and allowance of claims 36-61 is respectfully requested.

Respectfully submitted,

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